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EXAMINER	
HUYNH, PHUONG N	

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1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,108	QASBA ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,43-45 and 49* is/are pending in the application.

4a) Of the above claim(s) *4-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8-10,43-45 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-10, 43-45 and 49 are pending.

2. Claims 4-7 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. The listing of references in the specification at page 50-53 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

4. The rejection of claims 1-3, 8, and 43-45 under 35 U.S.C. 102(b) as being anticipated by US Pat No. 5,608,060 (of record, issued March 4, 1997; PTO 892) has been obviated by the claims amendment filed March 12, 2009.

5. The rejection of claims 1-3, 8-10, 43-45 and 49 under 35 U.S.C. 102(e) as being anticipated by US Pat No. 7,265,085 (issued Sept 4, 2007; claimed priority to earliest provisional application 60/328,523 filed Oct 10, 2001; PTO 892) has been obviated by the claims amendment filed March 12, 2009.

6. The rejection of claims 1-3, 8-10, 43-45 and 49 under 35 U.S.C. 102(e) as being anticipated by US Pat No. 7,265,085 (issued Sept 4, 2007; claimed priority to earliest provisional application 60/328,523 filed Oct 10, 2001; PTO 892) has been obviated by the claims amendment filed March 12, 2009.

7. The rejection of claims 1 and 8-12 under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 7,265,085 (issued Sept 4, 2007; claimed priority to earliest provisional application 60/328,523 filed Oct 10, 2001; PTO 892) in view of Hang et al (J Am Chem 123: 1242-1243, 2001; PTO 1449) and Nauman et al (Biochimica et Biophysica Acta 1568: 147-154, 2001; PTO 892) has been obviated by the claims amendment filed March 12, 2009.

8. In view of the amendment filed March 12, 2009, the following rejections remain.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-3, 8-10, 43-45 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method of making targeted glycoconjugate comprising a specific bioactive agent and a specific targeting compound wherein the bioactive agent and the targeting compound are joined by a modified UDP galactose-Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring using the mutant Y289L galactose transferase for detection assays, **does not** reasonably provide enablement for (1) any targeted glycoconjugate comprising any bioactive agent and any targeting compound, any targeting compound is any glycoprotein wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound wherein said modified saccharide compound comprises galactose and any reactive functional group, any functional group such as ketone group attached to the C2 position of the galactose ring for use in any medical therapy as set forth in claims 1-3, 8-12, 45 and 49, (2) any pharmaceutical composition comprising any unspecified glycoconjugate mentioned above and a pharmaceutical acceptable carrier as set forth in claim 43, (3) a kit comprising any unspecified targeted glycoconjugate for use in any therapeutic method or diagnostic method as set forth in claims 44-45. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The claims encompass innumerous targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound for use in any and all medical therapy.

Enablement is not commensurate in scope with how to use any unspecified targeted glycoconjugate comprising any bioactive agent and any targeting compound, any targeting compound is any glycoprotein wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound wherein said modified saccharide compound comprises galactose and any reactive functional group, any functional group such as ketone group attached to the C2 position of the galactose ring for any and all medical therapy or diagnosis.

The specification discloses only labeling of CREB or bovine lens α-crystallin using recombinant O-GlcNAc glycosylated CREB and the mutant Y289L O-GlcNAc glycosyltransferase, see pages 45-46. The specification discloses only modified UDP galactose--Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring because the mutant Y289L galactose transferase has been shown to tolerate unnatural substrates containing minor substitution at the C-2 position, including 2-deoxy, 2-amino, and 2-Acetyl substituents, see page 48 of the specification and summary of the specification.

The intended use of the claimed the unspecified glycoconjugate is for any and all therapeutic or diagnostic method (claims 44-45). When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation. See *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (claiming a chimeric gene capable of being expressed in any cyanobacterium and thus defining the claimed gene by its use), see MPEP 2164.01(c).

In this case, the specification provided little or no guidance as to the binding specificity of the targeting compound beyond the mere mentioned of a laundry list of targeting molecules, bioactive agents joined by a list of modified saccharide compounds. The specification merely asserts that the claimed treat numerous diseases including AIDS, see page 30 of specification. There is no guidance as to the binding specificity of the targeting compound for the claimed glycoconjugates. Given the numerous unspecified glycoconjugates, there is a lack of *in vivo* working example of such glycoconjugate could treat any diseases such as AIDS. As such, it is unpredictable which disease(s) could be treated by the claimed glycoconjugate.

Further, pharmaceutical composition in the absence of *in vivo* data are unpredictable for the following reasons: (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for *in vivo* therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

The specification does not adequately teach how to effectively treat any diseases or diagnosing any diseases using any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide without guidance as to the binding specificity of such glycoconjugate to the development of effective in vivo human therapeutic compositions, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the conjugate exemplified in the specification or the breadth of glycoconjugate for treating any diseases, encompassed by the claims.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed March 12, 2009 have been fully considered but are not found persuasive.

Applicants' position is that the claims have been amended to recite a reactive functional group attached to the C2 position of galactose, wherein the reactive functional group is selected from an amino, hydroxy, carboxyl, thiol, phosphate, phosphinate, ketone, sulfate or sulfate group.

The claims have been amended to recite that the saccharide is galactose. The specification provides teaching, for example at page 9, directed to "Modified Sacharide Compounds." In particular, the specification teaches that the glycoconjugates are constructed from their individual components, e.g., targeting compound (T), donor molecule including a saccharide residue (S), and bioactive agent (B) (p.9) Galactose is a well known saccharide to any person skilled in the art. The Specification teaches that the C2 position is favorable over other positions on the galactose ring because GalT has been shown to tolerate unnatural substrates containing minor substitutions at the C2 positions. For example, at page 48 of the specification, Applicants describe a strategy for the rapid mad sensitive detection of O-GlcNAc glycosylated proteins, where experiments show that C2 ketone functionality was appended at the C-2 position of the galactose ring because GalT has been shown to tolerate unnatural substrates containing minor substitutions at the C-2 positions, including 2-deoxy, 2-amino, and 2-N-acetyl substituents (Inn et al., 2001; Wong et el., 1995) (and)... 2-deoxy-Gal was transferred at rates comparable to Gel, whereas 3-, 4, and 6-deoxy-Gal were transferred at reduced rates." (page 48).

In response, the claims are not drawn to a method making targeted glycoconjugate from their individual components such as bioactive agent and targeting compound joined by a modified saccharide compound which comprises galactose and reactive functional group attached to the C2 position of the galactose ring. Amended claim 1 still recites a targeted glycoconjugate comprising a bioactive agent and a targeting compound, wherein the bioactive agent and targeting compound are joined by a modified saccharide compound, and wherein the modified saccharide compound comprises galactose and a reactive functional group attached to the C2 position of the galactose ring. The claims encompass any targeted glycoconjugate comprising any and all bioactive agent and any and all targeting compound, wherein the bioactive agent and targeting compound are joined by any modified saccharide compound, and wherein the modified saccharide compound comprises galactose and any reactive functional group attached to the C2 position of the galactose ring for use in therapeutic or diagnostic or medical therapy. None of the claims recites the specific glycoconjugate comprising the specific bioactive agent and the specific targeting compound joined by the modified galactose at the C-2 position of galactose ring.

Enablement is not commensurate in scope with how to use any unspecified targeted glycoconjugate comprising any bioactive agent and any targeting compound, any targeting compound is any glycoprotein wherein the bioactive agent and the targeting compound are joined

by any modified saccharide compound wherein said modified saccharide compound comprises galactose and any reactive functional group, any functional group such as ketone group attached to the C2 position of the galactose ring for any and all medical therapy or diagnosis.

The specification discloses only labeling of CREB or bovine lens α-crystallin using recombinant O-GlcNAc glycosylated CREB and the mutant Y289L O-GlcNAc glycosyltransferase, see pages 45-46. The specification discloses only modified UDP galactose--Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring because the mutant Y289L galactose transferase has been shown to tolerate unnatural substrates containing minor substitution at the C-2 position, including 2-deoxy, 2-amino, and 2-Acetyl substituents, see page 48 of the specification and summary of the specification.

The intended use of the claimed the unspecified glycoconjugate is for any and all therapeutic or diagnostic method (claims 44-45).

As stated in the MPEP, when a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation. See *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (claiming a chimeric gene capable of being expressed in any cyanobacterium and thus defining the claimed gene by its use), see MPEP 2164.01(c).

In this case, the specification provided little or no guidance as to the binding specificity of the targeting compound beyond the mere mentioned of a laundry list of targeting molecules, bioactive agents joined by a list of modified saccharide compounds. The specification merely asserts that the claimed treat numerous diseases including AIDS, see page 30 of specification. There is no guidance as to the binding specificity of the targeting compound for the claimed glycoconjugates. Given the numerous unspecified glycoconjugates, there is a lack of *in vivo* working example of such glycoconjugate could treat any diseases such as AIDS. As such, it is unpredictable which disease(s) could be treated by the claimed unspecified glycoconjugate.

Further, pharmaceutical composition in the absence of *in vivo* data are unpredictable for the following reasons: (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has

no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for *in vivo* therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

The specification does not adequately teach how to effectively treat any diseases or diagnosing any diseases using any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide without guidance as to the binding specificity of such glycoconjugate to the development of effective in vivo human therapeutic compositions, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the conjugate exemplified in the specification or the breadth of glycoconjugate for treating any diseases, encompassed by the claims.

11. Claims 1-3, 8-10, 43-45 and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 1, 9 and 45 are broadly drawn to any targeted glycoconjugate comprising any and all bioactive agent and any and all targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound wherein the modified saccharide comprises galactose and any reactive functional group attached to the C2 position of the galactose ring for use in any medical therapy.

Claim 2 is broadly drawn to any targeted glycoconjugate comprising any bioactive agent such as any and all polypeptide, any and all releasing factor, any and all releasing factor inhibitor, any and all carbohydrate, any and all nucleic acid and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound wherein the modified saccharide comprises galactose and any reactive functional group attached to the C2 position of the galactose ring for use in any medical therapy.

Claim 3 is broadly drawn to any targeted glycoconjugate comprising any bioactive agent and any targeting compound such as any and all glycoprotein wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound wherein the modified

saccharide comprises galactose and any reactive functional group attached to the C2 position of the galactose ring for use in any medical therapy.

Claim 8 is broadly drawn to any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound such as galactose wherein the modified saccharide comprises galactose and any reactive functional group attached to the C2 position of the galactose ring for use in any medical therapy.

Claim 10 is broadly drawn to any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified galactose comprises galactose and any reactive functional group ketone attached to the C2 position of the galactose ring for use in any medical therapy.

Claim 43 is broadly drawn to any and all pharmaceutical composition comprising any and all any targeted glycoconjugate comprising any and all bioactive agent and any and all targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound wherein the modified saccharide comprises galactose and any reactive functional group attached to the C2 position of the galactose ring and a pharmaceutically acceptable carrier for use in any medical therapy.

Claim 44 is broadly drawn to a kit comprising any and all targeted glycoconjugate comprising any and all bioactive agent and any and all targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound wherein the modified saccharide comprises galactose and any reactive functional group attached to the C2 position of the galactose ring for use in any therapeutic or any diagnostic methods.

Claim 49 is broadly drawn to a targeted glycoconjugate comprising any and all bioactive agent and any and all targeting compound, wherein the bioactive agent and targeting compound are joined by a modified saccharide compound, and wherein the modified saccharide compound comprises galactose and a reactive functional group attached to the C2 position of the galactose ring, wherein the reactive functional group is a ketone group.

The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties of targeting compound and bioactive agent such as widely differing amino acid sequences, nucleotide sequences, and biological functions in the

claimed glycoconjugate. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provides only the bovine sequence.

In this case, the specification does not reasonably provide a **written description** for the structure associated with function of any bioactive agent, and the structure associated with function of any targeting compound in the claimed glycoconjugate for use in any medical therapy.

At the time of filing, the specification discloses only labeling of CREB or bovine lens α-crystallin using recombinant O-GlcNAc glycosylated CREB and the mutant Y289L O-GlcNAc glycosyltransferase, see pages 45-46. The specification discloses only modified UDP galactose--Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring because the mutant Y289L galactose transferase has been shown to tolerate unnatural substrates containing minor substitution at the C-2 position, including 2-deoxy, 2-amino, and 2-Acetyl substituents, see page 48 of the specification and summary of the specification.

At the time of filing, applicants are not in possession of a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound for use in any medical therapy or any diagnostic method. The specification provided little or no guidance as to the *binding specificity* of the targeting compound beyond the mere mentioned of a laundry list of targeting molecules; the structure associated with function of any and all bioactive agents joined by any modified saccharide compounds comprising galactose. The specification merely asserts that the claimed treat numerous diseases including AIDS, see page 30 of specification. There is no guidance as to the binding specificity of the targeting compound in the claimed glycoconjugates. There is no disclosure of any *in vivo* working example that the claimed glycoconjugate could treat any disease such as AIDS, cancer, any autoimmune diseases, any bacterial infections, any psychiatric diseases, any cardiovascular diseases, etc. In this case, the specification fails to disclose a representative number of species of each claimed genus, which includes many members with widely differing structural, chemical, and biological functions. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the specific modified galactose residue having a ketone group at C2 position of the galactose linked to a specific targeting agent and a specific bioactive agent using the specific recombinant mutant Y289L galactose transferase for detection assays, the skilled artisan cannot envision the detailed chemical structure of the encompassed glycoconjugate and binding specificity of the targeting compound for treating or diagnosing any diseases. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel,* 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Further, possession may not be shown by merely described how to obtain possession of members of the claimed genus or how to identify their common structural features. See University of Rochester, 358 F.3d at 927, 69 USPQ2d at 1895.

Because the described labeling of CREB or bovine lens α-crystallin involving modified galactose residue having a ketone group at C2 position of the galactose made by using the specific recombinant mutant Y289L galactose transferase for detection assays is not representative of the entire claimed genus of targeted glycoconjugate comprising a genus of bioactive agent such as any polypeptide, any releasing factor, any releasing factor inhibitor, any carbohydrate any nucleic acid linked to any targeting compound via modified saccharide comprising galactose having any functional group attached at the C2 position of the galactose ring for treating any diseases, one of skill in the art would conclude that applicant was not in procession of the claimed genus of targeted glycoconjugate. Therefore, the specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claims 1-3, 8-10, 43-45 and 49 mentioned above.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001and revision of the Written Description Training materials, posed April 11, 2008 http://www.USPTO.gov/web/menu/written.pdf.

Applicants' arguments filed March 12, 2009 have been fully considered but are not found persuasive.

Applicants' position is that as amended, the claims are sufficiently described in the specification. Targeted glycoconjugate compounds are described at page 8. Modified saccharide compounds arc described at page 9. Targeting compounds are described at page 10, page 18. Bioactive agents arc described beginning at page 10.

In response, amended claims are broadly drawn to any targeted glycoconjugate comprising any and all bioactive agent and any and all targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound wherein the modified saccharide comprises galactose and any reactive functional group attached to the C2 position of the galactose ring for use in any medical therapy.

The specification described only labeling of CREB or bovine lens α-crystallin using modified galactose residue having a ketone group at C2 position of the galactose made by using the specific recombinant mutant Y289L galactose transferase for detection assays.

There is insufficient description about the binding specificity associated with structure of the targeting compound in the claimed glycoconjugate. There is also a lack of disclosure as to the structure associated with function of the "bioactive agent", bioactive agent such as any polypeptide without the amino acid sequence, any releasing factor, any releasing factor inhibitor, any carbohydrate, any nuclei acid without the nucleic acid, any vaccine, any antagonist, any enzyme inhibitor, any herbal remedy etc.

There is no showing of any glycoconjugate comprising the unspecified bioactive agent and unspecified targeting compound could be used to treat any unspecified disease. The specification provided little or no guidance as to the *binding specificity* of the targeting compound beyond the mere mentioned of a laundry list of targeting molecules; the structure associated with function of any and all bioactive agents joined by any modified saccharide compounds comprising galactose other than O-GlcNAc. The specification merely asserts that the claimed treat numerous diseases including AIDS, see page 30 of specification. There is no guidance as to the binding specificity of the targeting compound in the claimed glycoconjugates. There is no disclosure of any *in vivo* working example that the claimed glycoconjugate could treat any disease such as AIDS, cancer, any autoimmune diseases, any bacterial infections, any psychiatric diseases, any cardiovascular diseases, etc. In this case, the specification fails to disclose a representative number of species of each claimed genus, which includes many members with widely differing structural, chemical, and biological functions. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus.

12. The following new ground of rejection is necessitated by the amendment filed March 12, 2009.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1-3, 8-10, 43-45 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 7,265,085 (of record, issued Sept 4, 2007; claimed priority to earliest provisional application 60/328,523 filed Oct 10, 2001; PTO 892) in view of Ramakrishnan et al (J Biol Chem 277(23): 20833-20839, June 2002; PTO 892) and Hang et al (of record, J Am Chem 123: 1242-1243, 2001; PTO 1449).

The '085 patent teaches various targeted glycoprotein such as transferrin-SA linker-GDNF wherein the reference targeting compound such as transferrin and bioactive agent such as GDNF are joined by a modified saccharide compound such o-Glc-NAc modified galactose using β-1,4 galactosyl transferase (see col. 349-350, claims 1-4 of '085 patent, back ground of invention, in particular). The reference modified saccharide is galactose or Gal (see summer of invention, paragraph 68, in particular). The modified saccharide or modified sugar such as glycosyl residues have also been modified to contain ketone groups (see paragraph 26, Background of invention, paragraphs 579-592, in particular). The reference modified or oxidized galactose may further comprise a terminal galactose residue to the corresponding aldehyde, see paragraph 25, in Back ground of invention, in particular). The '085 patent also teaches a pharmaceutical composition comprising the reference glycoconjugate and a pharmaceutical acceptable carrier such as PBS or saline (see paragraphs 1189-1193, in particular). The '085 patent also teaches a kit comprising the reference glycoconjugate and instructions for how to use

such glycoconjugate (see paragraph 1450, in particular). The '085 patent further teaches glycopeptide molecule having a modified sugar molecule or other compound conjugated thereto confers a beneficial property on the peptide; the conjugate molecule is added to the peptide enzymatically because enzyme-based addition of conjugate molecules to peptides has the advantage of regioselectivity, stereoselectivity and having desired and or modified glycan structures that can be produce at an industrial scale for the efficient production of improved therapeutic peptides (see summary of invention).

The invention differs from the teachings of the reference only in that the glycoconjugate wherein the reactive functional group is attached to the C2 position of the saccharide ring instead of any position in the saccharide ring.

The invention in claim 12 differs from the teachings of the reference only in that the glycoconjugate wherein the reactive functional group is attached to the C2 position of the galactose ring instead of any position in the galactose ring.

Ramakrishman et al teach a modified β1,4-galactosyltransferase (β4Gal-T1) having a tyrosine at position 289 substitute for Lysine that enhances the GalNAc-transferawse activity equal to that of Gal-T activity (see entire document, page 20837, col. 1, page 20836, col. 1, in particular). The reference modified enzyme creates the required optimal space between the keto group of C2 atom of galactose (Gal) and the side chain of Tyr-289 enzyme creating a site specific conjugation (see FIG 22A-C, in particular).

Hang et al teach the use of unnatural or modified monosaccharide such as 2-ketosugars or 2-keto isostere of GalNAc (galacto-N-Acetyl) sugar or 2-N-acetaminodugars as the substrate for GalNAc transferase for metabolic glycoprotein engineering in CHO cells; the 2-Keto GalNAc might be exploited to introduce unique chemical reactivity into secreted glycoproteins produced by large-scale recombinant expression, allowing further selective modification (see page 1243, col. 2, last paragraph, in particular). Hang et al further teach the ketone reactive group produced by 2-ketosugars can be used as a molecular handle and more accessible for chemical reaction with biotin hydrazide (see page 1243, col. 1-2, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the β-1,4 galactosyl transferase that catalyze the transfer of galactose in the target conjugate of the '085 patent for the modified β1,4-galactosyltransferase (β4Gal-T1) that catalyze the transfer of galactose from UDP-Gal to the N-acetylglucosamine (GlcNAc) at the C2 ketone of galactose as taught by Ramakrishman et al using any modified

monosaccharide such as 2-ketosugars or 2-keto isostere of GalNAc (galacto-N-Acetyl) as a molecular handle as taught by Hang et al.

One having ordinary skill in the art would have been motivated with the expectation of success to substitute the naturally occurring β-1,4 galactosyl transferase in the method of making target conjugate of the '085 patent for the modified β1,4-galactosyltransferase (β4Gal-T1) having a tyrosine at position 289 substitute for Lysine as taught by Ramakrishman et al because the modified β1,4-galactosyltransferase (β4Gal-T1) enzyme has enhances the GalNAc-transferawse activity equal to that of unmodified Gal-T activity in addition to site specific recognition of the ketone group in the C2 position of the galactose (see entire document, page 20837, col. 1, page 20836, col. 1, in particular).

One having ordinary skill in the art would have been motivated to do use 2-ketosugars or 2-keto isostere of GalNAc (galacto-N-Acetyl) sugar or 2-N-acetaminodugars as the substrate for conjugation because Hang et al teach the 2-Keto GalNAc might be exploited to introduce unique chemical reactivity into secreted glycoproteins produced by large-scale recombinant expression, allowing further selective modification (see page 1243, col. 2, last paragraph, in particular). One having ordinary skill in the art would have been motivated to do use 2-ketosugars or 2-keto isostere of GalNAc (galacto-N-Acetyl) sugar or 2-N-acetaminodugars as the substrate for conjugation because Hang et al teach the ketone group can be used as a molecular handle and more accessible for chemical reaction with biotin hydrazide (see page 1243, col. 1-2, in particular).

One having ordinary skill in the art would have been motivated with the expectation of success to make and use site specific conjugation of glycoconjugate for drug delivery because the '085 patent teaches enzyme-based addition of conjugate molecules to peptides has the advantage of regioselectivity, stereoselectivity and can be produce at an industrial scale for the efficient production of improved therapeutic peptides (see summary of invention). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Applicants' arguments filed March 12, 2009 have been fully considered but are not found persuasive.

Applicants' position is that the '085 patent provides no teachings or suggestion that a modification at the C2 position of the saccharide ring is preferable over any position in the saccharide ring and it would not be obvious to one of ordinary skill in the art at the time the

invention was made to substitute the linker substrate of O-linked SA modified galactose of the '085 patent for the 2-ketosugars or 2-ketoisostere of GalNAc as taught by Huang where the ketone bearing sugar can react with a number of nucleophiles.

In response, Ramakrishman et al teach modification at the C2 position of the saccharide ring using a modified β1,4-galactosyltransferase (β4Gal-T1) having a tyrosine at position 289 substitute for Lysine that enhances the GalNAc-transferawse activity equal to that of Gal-T activity (see entire document, page 20837, col. 1, page 20836, col. 1, in particular). The reference modified enzyme creates the required optimal space between the keto group of C2 atom of galactose (Gal) and the side chain of Tyr-289 enzyme creating a site specific conjugation (see FIG 22A-C, in particular).

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The IFW official Fax number is (571) 273-8300.

19. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
July 2, 2009